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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,359	06/23/2005	Eva Altmann	PA/4-32832A	3331

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

NOTIFICATION DATE	DELIVERY MODE
07/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/540,359	ALTMANN ET AL.	
	Examiner	Art Unit	
	TAMTHOM N. TRUONG	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4-23-08 (Election)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/31/08 + 6/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL ACTION

It is acknowledged that applicants have elected without traverse Group I (claims 1, 2 and 5-9) drawn to compounds of formulae I or I', pharmaceutical compositions and methods for making same.

Claims 3, 4 and 10 are withdrawn as being drawn to the non-elected subject matter.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1, 2 and 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. In the definitions of R1, R2 and R3, it is unclear if the moieties in parentheses are part of the claim.

b. The term "preferably" (used throughout claims 1 and 2) renders the claims indefinite because it is not clear which moiety is intended.

c. The extensive list of provisos in claims 1 and 2 renders those claims and claims dependent thereon indefinite because the provisos attempt to "claim the invention by excluding what the inventors did not invent rather than distinctly and particularly pointing out what they did invent." **In re Schechter,** 205 F. 2d 185, 98 USPQ 144 (CCPA 1953).

d. In claim 9, the limitation of "if required converting the R1, R2 or R3 residues into alternative R1, R2 or R3 residues to give an alternative compound of formula I" renders the claim indefinite because it is not clear which compound is converted into which.

e. Claim 5 is a substantial duplicate of claim 1 because the intended use does not result in structural change of the formula in claim 1.

f. **Use Claim:** Claim 6 provides for the use of a compound according to claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. **Use Claim:** Claim 6 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of **osteoporosis** (various types) and **osteopathy**, does not reasonably provide enablement for other disorders such as: seizures, stroke, head trauma, various psychological disorders (depression, anxiety, schizophrenia, etc.). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;
(2) The amount of direction or guidance presented;
(3) The state of the prior art;
(4) The relative skill of those in the art;
(5) The predictability or unpredictability of the art;
(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 6-8 recite a scope of diseases including bone conditions, seizures, stroke, head trauma, spinal cord injury, hypoxia-

induced nerve cell damage, epilepsy, neurodegenerative diseases, Alzheimer's disease, Huntington's disease and Parkinson's disease, dementia, muscle tension, depression, anxiety, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, schizophrenia, neuroleptic malignant syndrome, congestive heart failure; hypertension; gut motility disorders, diarrhoea, spastic colon disorder, dermatological disorders, burns, ulcerations, wounds; osteoporosis, juvenile osteoporosis, menopausal osteoporosis, post-menopausal osteoporosis, post-traumatic osteoporosis, fractures, osteopathy, osteo-malacia, periodontal bone loss or bone loss due to arthritis or osteoarthritis or for treating hypoparathyroidism.

Note, the above diseases affect different organs and do not share the same etiology. Thus, the scope of the intended diseases is unduly broad.

The amount of direction or guidance presented: The specification only describes "Inositol Phosphate Formation Assay" and "Intracellular Free Calcium" which only provide evidence for the treatment of osteoporosis and osteopathy, but not for divergent diseases and conditions such as seizures, neurodegenerative diseases, Alzheimer's disease, Parkinson's disease, neuroleptic, malignant syndrome, congestive heart failure, etc. There is no data that the claimed compounds could improve mood, cognitive function, cardiovascular activity, GI motility, or alleviate seizures, burns, wounds, etc. Thus, except for osteoporosis and osteopathy, the specification fails to provide enablement for treatment for the remaining recited diseases an conditions.

The state of the prior art: It is well known that parathyroid hormone (PTH) is associated with bone metabolism. It stimulates the release of calcium from bones by increasing resorption of bone. Thus, any compound that antagonizes PTH receptor would inhibit the resorption of bones. In the instant case, the claimed compounds antagonize parathyroid calcium-

sensing receptor (or PcaR) which would inhibit bone resorption, and improve osteoporosis or osteopathy. Because there is no link between PcaR and other diseases, there is no basis to believe that the claimed compounds could treat an array of diseases recited in claims 6-8.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the large Markush group of the instant formula. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound in the treatment of each disease. Given a large Markush group of the instant formula and a myriad of diseases, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting path ways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the antagonistic activity on PcaR shown in two assays does not sufficiently enable the skilled clinician to treat the many diseases that are not related to bone resorption, or have different underlying factors.

See ***Hoffman v. Klaus*** 9 USPQ 2d 1657, and ***Ex parte Powers*** 220 USPQ 925 regarding type of testing needed to support *in vivo* uses.

Thus, with such a limited teaching and an unduly broad scope, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in recited in claims 6-8.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 2 and 8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25, 32 and 34 of U.S. Patent Application No. 10/480,559 (or AN'559--recently allowed). Although the conflicting claims are not identical, they are not patentably distinct from each other because formula IV of the allowed application (AN'559) is a subgenus of the instant formula I or I' with the following substituents:

a. R1 corresponds to R_1' of AN'559 and represents similar moieties such as: an alkenyl, an alkenyloxy, an alkynyl, an alkynyloxy group, etc.

b. R2 corresponds to R_3" of AN'559 and represents an alkyl group;

c. R3 corresponds to R_2" of AN'559 and represents a benzyl group substituted with an alkoxy group.

d. A species in claim 34 (e.g., the 6th species on page 6) of AN'559 reads on the instant formula I or I'.

Despite an extensive list of provisos, formula IV of AN'559 still has claims reciting overlapping subject matter with that of the instant formula I and/or I'.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 5 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the following references:

i. **Masai et. al.** (Chem. Pharm. Bull., Vol. 25 (1977), pp. 3018-3022. See compounds 3 through 12 on page 3018.

ii. **Gamboni et. al.** (US 4,236,006): See column 3, Example 3, compound (a).

iii. **Yamamoto et. al.** (US 4,202,974): See column 3, compounds on line 19 and line 26.

iv. **Yamamoto et. al.** (US 4,387,223): See column 4, compound on line 5 (i.e., the 3rd compound in column 4).

The above references disclose compounds that read on the instant formula I with the following substituents:

a. R1 is an alkyl or alkoxy group;

b. R2 is a halogen or alkoxy group;

c. R3 is an alkyl substituted with a cylcoalkyl group, or an alkyl group.

The disclosed compounds of Masai have anti-inflammatory property, and thus, the pharmaceutical composition recited in the instant claim 8 is also anticipated.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tamthom N. Truong/

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624

Tamthom N. Truong
Examiner
Art Unit 1624

6-10-08